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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,772	06/02/2005	William Alexander Denny	4450-14	1493

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EXAMINER	
KOSACK, JOSEPH R	
ART UNIT	**PAPER NUMBER**
1626	
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02/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,772	DENNY ET AL.	
	Examiner	Art Unit	
	Joseph Kosack	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,8-11,16 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,8-11,16 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☑ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-4, 6, 8-11, 16, and 19 are pending in the instant application.

Amendments

The amendment filed on November 9, 2007 has been acknowledged and has been entered into the application file.

Previous Claim Rejections - 35 USC § 112

Claims 12-18 were rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. Applicant's amendments have resolved the issue and the rejection is withdrawn.

Claims 20-21 provided for the use of compounds of Formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. As the claims have been cancelled, the rejection is withdrawn.

Previous Claim Rejections - 35 USC § 101

Claims 20-21 were rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. As the claims have been cancelled, the rejection is withdrawn.

Previous Claim Rejections - 35 USC § 103

Claims 1-21 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over Friedlos et al. (*J. Med. Chem. 1997,* 1270-1275) in view of Patani et al. (*Chem. Rev. 1996,* 3147-3176).

Applicant has traversed the rejection on the grounds that the compound 6 of Friedlos et al. is the closest to the compounds of formula IIb of the instant invention and still have significant structural differences that cannot be resolved by the references, and that Friedlos et al. require A and B to be the same.

This is not found to be persuasive because the compounds that are closest to formula IIb are compounds 12-16 of Friedlos et al. The reason why the only compound that has A and B different in Friedlos et al, compound 6, is insufficiently potent is that it uses chlorine and mesylate, which from the data of Friedlos et al. are consistently the least potent substituents for this system. There would be and expectation of success if a chlorine is replaced with bromine or iodine that a more potent drug would be realized. Therefore, there is a reasonable expectation of success to develop an active drug with the teachings of Friedlos et al. and Patani et al. The rejection is maintained for claims 1, 3-4, 6, 8-11, 16, and 19, and is withdrawn for all cancelled claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

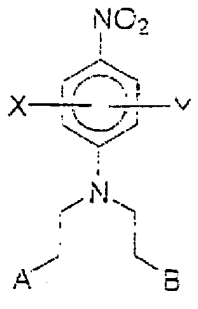
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

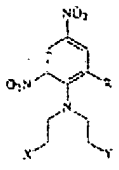
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-4, 6, 8-11, 16, and 19 rejected under 35 U.S.C. 103(a) as being unpatentable over Friedlos et al. (*J. Med. Chem. 1997,* 1270-1275) in view of Patani et al. (*Chem. Rev. 1996,* 3147-3176).

The instant application is drawn compounds of Formula I: 

, their method of making, their method of use to treat tumors and cancer via GDEPT, and their use for the manufacture of medicaments.

Determination of the scope and content of the prior art (MPEP §2141.01)

Friedlos et al. teach compounds of the formula  where R is $CONH_2$ and X and Y can be the same where they are halo. See Table 2 on page 1272. Friedlos et al. also details the method of making the halo substitution from the mesylate by reacting with a sodium halide in ethyl acetate. See page 1273, column 2. Finally, Friedlos teaches the method of treating of cancerous cells via GDEPT and a nitroreductase enzyme from E. Coli. See page 1274, column 2. As the compound is used as a medicament, the use of making a medicament is inherently described.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Friedlos et al. do not teach compounds in line with the proviso in which A ≠ B.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Patani et al. teach that chlorine can be replaced by bromine or iodine. See page 3148, Table 3. This would yield 2(-[6-(Aminocarbonyl)(2-bromoethyl)-2,4-dinitroanilino]ethyl methaneiodide.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to follow the synthetic scheme of Friedlos et al. with the replacement suggested by Patani et al. to make the claimed invention. The motivation to do so is provided by Patani et al. Patani et al. teach the use of bioisosteric replacements to rationally modify lead compounds into safer and more clinically effective agents. See page 3147.

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

Conclusion

Claims 1, 3-4, 6, 8-11, 16, and 19 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Kosack whose telephone number is (571)-272-5575. The examiner can normally be reached on M-Th 6:30 A.M. until 5:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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